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A guideline-based decision support for pharmacological treatment can improve the quality of hyperlipidemia management

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ABSTRACT

Introduction: The Institute of Medicine has identified both Computerized Physician Order Entry (CPOE) and Electronic Prescription (EP) as key in reducing medication errors and improving safety. Many computerized clinical decision support systems (CDSSs) improve practitioner performance. However, the development of CDSSs involves a long cycle time that makes it difficult to apply in a wider scope.

Methods: In this study, we integrated the hyperlipidemia treatment guideline ATP III (Adult Treatment Panel III) in a CPOE of a medical center. The first 200 consecutive patients followed up more than 1 year were recorded for analysis.

Results: Our study revealed that 130 (65%) patients reached the LDL-C (low density lipoprotein-cholesterol) goal in 1 year. For those who with CDSS finished, 74% reached the LDL-C goal. For those who with CDSS exited, 57% reached the LDL-C goal. The odds ratio is 2.1 (1.2, 3.8) ($p = 0.022$), which means for those who with CDSS finished can have 2 times of chance to reach the LDL-C goal. The mean of days to attain the LDL-C goal level after initiation of antihyperlipidemia therapy was 175 ± 98 days. 11,806 prescribing records from 8023 patients were collected for analyzing the reasons of prematurely exiting the CDSS. The most frequent reason for exiting the system is “too busy to use”.

Conclusion: We conclude that a CPOE with CDSS integrated may let more hyperlipidemia patients reach the LDL-C goal. However, data also showed the total prescribing time may increase. The results of a preliminary evaluation are presented to illustrate that the CDSSs can improve the quality of hyperlipidemia management.

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1. Introduction

The Institute of Medicine (IOM) and the Agency for Healthcare Research and Quality (AHRQ) have recommended clinical practice guidelines (CPG) to improve the quality of patient care [1,2]. A clinical practice guideline is a systematically developed statement for practitioners and patients to establish an appropriate healthcare plan for a specific clinical condition. A good clinical guideline should be valid, reproducible, cost-effective, representative, multidisciplinary, clinically applicable, flexible, clear, reviewable, and amenable to clinical audit [3]. CPG provides a standard method and/or a collection of clinical experiences as a reference to help physicians dealing with a specific situation upon diagnosis.

IOM has set a goal for the medical delivery system in the next decade. That is, by the year 2020, 90% of clinical decisions will be supported by accurate, timely, and up-to-date clinical information, and will reflect the best available evidence [4]. Quality indicators are used for assessing the deficits in adherence to recommended processes. For example, care requiring a medication had the adherence rates of 69% only [5]. Strategies to reduce these deficits in health care are warranted.

It is challenging to raise the guideline compliance rate of physicians. It is sometimes too complicated or impossible to follow the steps in each guideline, especially when the local standard has been established already [6,7]. Concerning this matter, the guideline may not be fully used to provide the greatest help on the medical treatment; even it contains abundant experiences and the best treatment. For example, the Agency for Health Care Policy and Research (AHCPR) heart failure guideline does not clearly define the symptoms and adverse events, which also cannot account for comorbid conditions [6,8].

The IOM has identified both Computerized Physician Order Entry (CPOE) and Electronic Prescription (EP) as key in reducing medication errors and improving safety [1]. Study revealed that a CPOE system with clinical decision support system (CDSS) integrated can much improve the outcome of practitioners' performance which is mainly measured by adherence to recommended guidelines [9]. The CDSS is a computer application that processes and analyzes the collected data and presents it so that the user can easily determine the best strategy and make a decision. However, there is still the possibility that it will be of no help to the user, or confound the user who is trying to make a decision.

Historically, much of the development of guidelines has occurred in the period around the 1970s. More recently, efforts are aimed at computer-based interpretation with the goal of delivering patient-specific recommendations at the point of care to reduce error rate and save time. Guidelines thus act as the core knowledge for these decision support applications.

Decision making on anti-hyperlipidemia medication is a relatively complicated process which requires data of the patient profile, medical history, laboratory and the present medication. Without the help of CDSSs, physician should find blood lipid data manually, and considers several risk factors at a time when prescribing. The Adult Treatment Panel III (ATP III) of the National Cholesterol Education Program (NCEP) issued an evidence-based guideline on cholesterol management

which is deemed as the standard of anti-hyperlipidemia treatment [10–13]. The NCEP is a program managed by the National Heart, Lung and Blood Institute, a division of the National Institutes of Health. Its goal is to reduce increased cardiovascular disease rates due to hypercholesterolemia (elevated cholesterol levels) in the United States of America. However, a study revealed that only 48.6% (44.1%, 53.2%) of the patients with hyperlipidemia received the recommended care [5].

A systematic review on effects of CDSSs on practitioner performance and patient outcomes revealed that the CDSSs improved practitioner performance in 62 (64%) of the 97 studies [9]. On the other hand, the effects on patient outcomes remain understudied and, when studied, inconsistent. Therefore, our study try to show CDSS can possibly shorten to duration to reach the LDL-C (low density lipoprotein-cholesterol) goal for hyperlipidemia patients. In fact, only 50% of commercial health plans met the LDL-C goal [14].

To help physicians make use of the guideline, an ATP III guideline integrated CPOE named CAGES (computer assisted guideline enhancement system) has been established to enhance the clinical decision support process and improve the quality of hyperlipidemia management.

2. Methods

CAGES, which was written in Java (Version 1.4, Sun Microsystems, Inc., USA) and Delphi tool (Version 5.0, Borland Software Corporation, Rockville, MD, USA) has been built in a medical center (Wan Fang Medical Center, Taiwan) since 2003."

The rule of the system is designed in a way that when a physician opens a electronic record of a patient, the abnormal data will pop out to remind the physician that the patient could be one of the hyperlipidemia cases. When the previous laboratory data reveal abnormal figures ($LDL-C \geq 130 \text{ mg/dL}$ or $TC \geq 200 \text{ mg/dL}$) (TC, total cholesterol), a red colored text will be shown to the physician [10,11]. Hyperlipidemia medication cannot be prescribed only according to abnormal laboratory data. There are some risk factors to consider and trying to change life style before taking the medicine. Therefore, when the anti-hyperlipidemia drugs are being prescribed, the CAGES will be triggered acting as a reminder as in Fig. 1.

Once CAGES is triggered, the previous laboratory test data will be shown on the top of the main page of CAGES to assist the physician in determining the patient's condition. The laboratory data include TC, TG (triglycerol), HDL-C (HDL-C, high-density lipoprotein cholesterol), and LDL-C, which are calculated by the computer automatically. LDL-C is the major atherogenic lipoprotein and has long been identified as the primary target in cholesterol-lowering therapy. It has been strongly validated by recent clinical trials, which show the efficacy of LDL-lowering therapy on reducing risk for CHD (coronary heart disease) [10–13,15,16]. Physicians were asked to evaluate the risk by tick the risk factors.

The decision making algorithm steps are structured as the following steps (Fig. 2):

STEP 1: Trigger the system by order entering,

STEP 2: Identify the presence of clinical atherosclerotic disease that confers high risk on CHD.

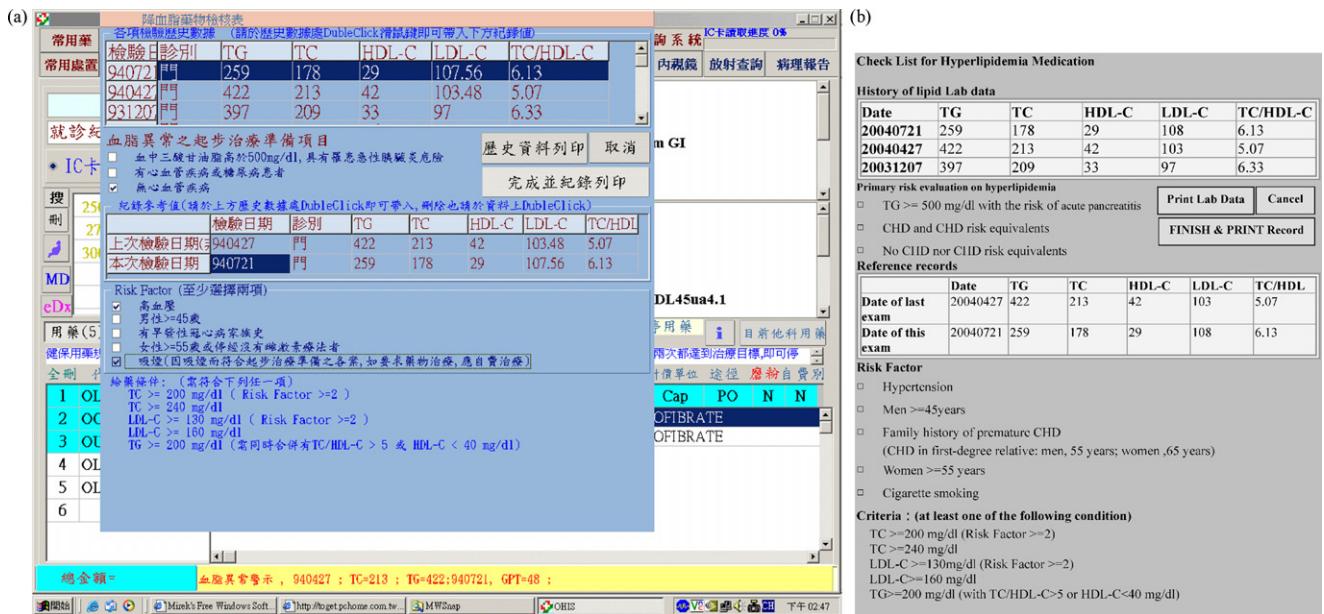


Fig. 1 – (a) The screenshot of the CDSS integrated CPOE. The laboratory data history is on the top of CDSS window. The part below is the initial therapy-prepared items. The third part is the laboratory data of these 2 times, following by the check items of the risk factors of hyperlipidemia. The last part is the criteria for medication. **(b)** The English translation of the CDSS window.

- STEP 3: Determine the major risk factors present,
- STEP 4: If more than two risk factors are present without CHD or CHD risk equivalent, then assess the 10-year (short-term) CHD risk,
- STEP 5: Determine risk category,
- STEP 6: Consider adding drug therapy if LDL-C exceeds levels,
- STEP 7: Confirm or reject the physician's order.

When the whole procedure of CAGES is done, a record is printed out automatically as a log for the physician. On the other hand, when the condition of the patient does not adhere to the treatment guideline, the order is rejected by the CDSS. Whenever the physician does not want to use this system, he or she can simply press the "Cancel" button to exit CAGES anytime, with a briefly specification for the reasons of quitting CAGES.

The first 200 consecutive patients followed up more than 1 year were recorded for analysis since August 2003. For those included, the average age is 65.7 years old. Sex ratio is 43:57 (F:M). Our study used LDL-C goal of ATP III [17]. The NECP has identified low-density lipoprotein cholesterol (LDL-C) as the primary target of cholesterol-lowering therapy [17]. According to the ATP III algorithm, persons are categorized into 3 risk categories: (1) established CHD and CHD risk equivalents, (2) multiple (2+) risk factors, and (3) zero to one (0–1) risk factor. CHD risk equivalents include noncoronary forms of clinical atherosclerotic disease, diabetes, and multiple (2+) CHD risk factors with 10-year risk for CHD >20%. All persons with CHD or CHD risk equivalents can be called high risk. In our study, all patients have ICD code 272 (dyslipidemia). Patients with ICD code 250 and 410–414 are included as high risk. Among our 200 patients, 150 are high risk, 50 are moderate risk. The ATP III

treatment goal of low-density lipoprotein cholesterol (LDL-C) >100 mg/dL is a disease specific quality indicator. In high-risk persons, the recommended LDL-C goal is >100 mg/dL. This therapeutic option extends also to patients at very high risk who have a baseline LDL-C < 100 mg/dL. For moderately high-risk patients (2+ risk factors and 10-year risk 10–20%), the recommended LDL-C goal is <130 mg/dL. Overall, it is advised that intensity of therapy be sufficient to achieve at least a 30–40% reduction in LDL-C levels.

3. Results

Among the first 200 consecutive patients followed up more than 1 year, 65% reached the LDL-C goal in 1 year (Table 1). These data is to analyze the effectiveness of the CDSS in terms of disease management. For those who with CAGES finished, 74% reached the LDL-C goal. For those who with CAGES exited, 57% reached the LDL-C goal. The odds ratio is 2.1 (1.2, 3.8) ($p = 0.022$), which means for those who with CAGES finished have 2 times of chance to reach the LDL-C goal in 1 year.

Our study showed the mean \pm SD number of days to attain the LDL-C goal level after initiation of statin therapy was 175 ± 98 days. Other study revealed that the mean of days to attain the LDL-C goal level after initiation of statin therapy was 189 ± 90 days [18]. The CDSS process was completed in 92 cases which spent 22 s more than those 108 patients who exited. The result support the conclusion of a study [19] which found CDSS in CPOE can increase total prescribing time due to the introduction of the CPOE system.

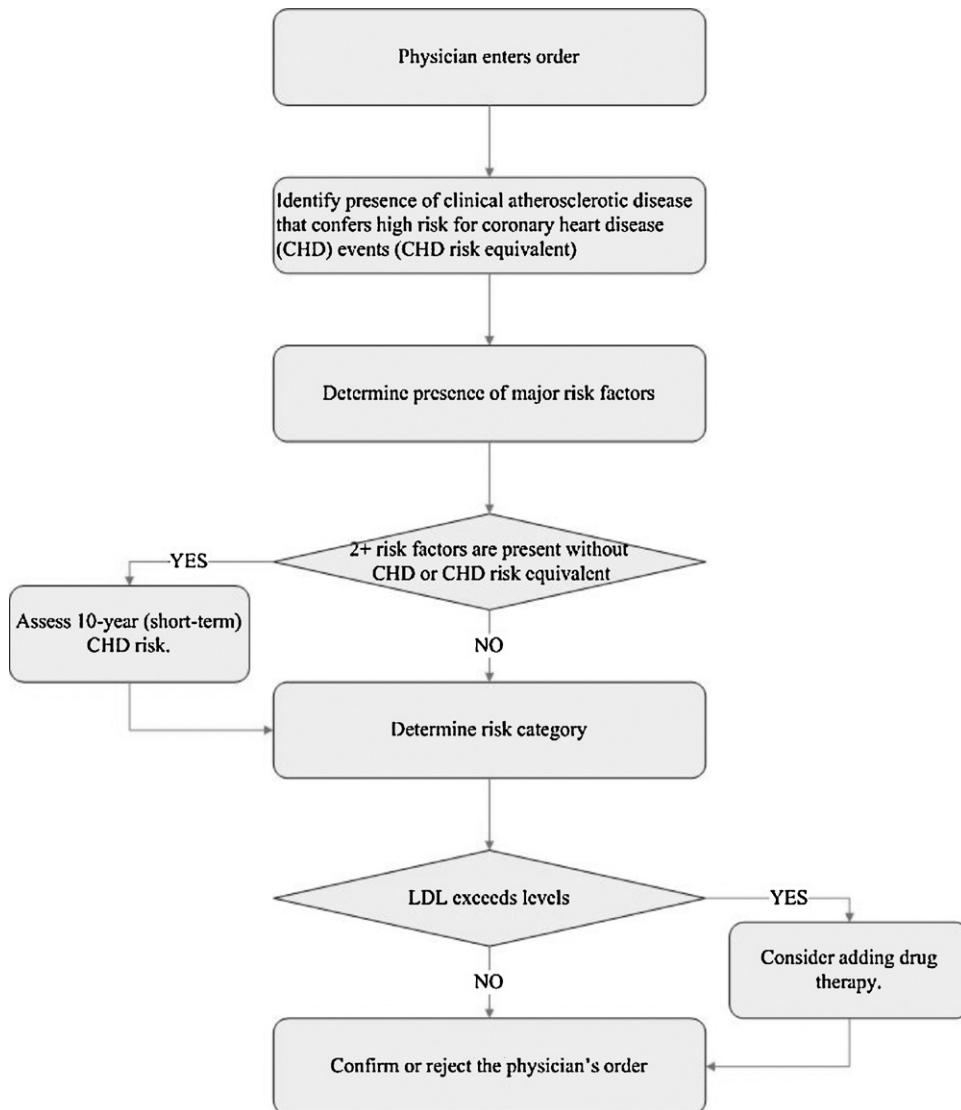


Fig. 2 – The decision making algorithm of CAGES.

Total 11,806 records from 8023 patients were collected from the CAGES in a period of 1 year and 9 months. These data is to demonstrate the overall usage of the system. 16.17% finished CAGES. The reason for exiting CAGES could be categorized into 4 parts.

Category 0: the doctor is too busy to use the program.

Category 1: the program is useless to the diagnosis.

Category 2: the guideline does not fit to the condition of the patient.

Category 3: other reasons.

The result of CAGES is shown in Fig. 3. The most frequent reason was “too busy to use”.

4. Discussion

We use the ATP III standards as quality indicator. The NCEP advocates aggressive LDL-C-lowering therapy for secondary prevention, with a goal of therapy to reduce LDL-C levels to 100 mg/dL (2.59 mmol/L) or less [20]. The National Committee for Quality Assurance (NCQA) is implementing a new performance measure as part of the Health Plan Employer

Table 1 – LDL goal analysis for the 200 patients (LDL goal +, the number of patients reach the LDL goal in 1 year) (LDL goal –, the number of patients fail to reach the LDL goal in 1 year).

| Finish CAGES (n = 92) | Exit CAGES (n = 108) | Total (n = 200) |
|-----------------------|----------------------|-----------------|
| LDL goal + | 68 (74%) | 130 (65%) |
| LDL goal – | 24 (26%) | 70 (35%) |

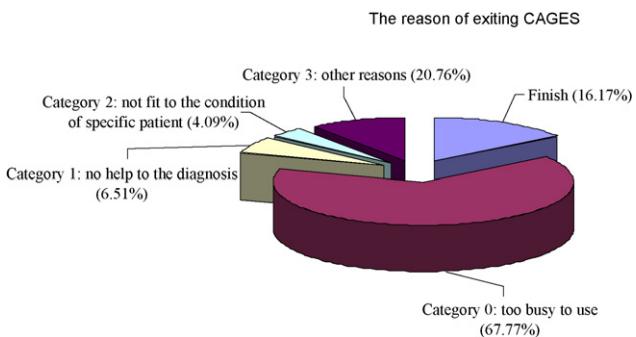


Fig. 3 – The result of CAGES.

and Data Information Set (HEDIS) that appears to endorse a hyperlipidemia treatment target [21]. The NCQA is an independent non-profit organization in the United States designed to improve health care quality. The HEDIS is a widely used set of performance measures in the managed care industry, developed and maintained by the NCQA. The new HEDIS measure will require managed care organizations seeking NCQA accreditation to measure and report the percentage of patients who have had major CHD events who achieve LDL-C levels less than 130 mg/dL (3.36 mmol/L) between 60 and 365 days after discharge. Our study showed that the guideline-based CDSS may shorten the days to attain the LDL-C goal level after initiation of statin therapy.

This study showed the largest part in the chart is “too busy to use” as Fig. 3. Other study also showed similar result as that clinicians’ main concern was that the CDSS would increase consultation times [22]. Nevertheless, the automatic calculation of the LDL data may save time and energy of the physicians in busy clinical work. The CAGES pushes laboratory data to CPOE at the time of ordering medication. They were appreciated with this function, and had shown great positive feedbacks from them. Lesson learned from other study showed that interoperability with other information systems is crucial to keep a CDSS being widely implemented [23].

The CAGES can improve clinical quality. Study showed a CDSS that is capable of applying the evidence-based rules extracted from guidelines regarding drug treatment suggesting an improvement of treatment quality [24]. Now, we have implemented one guideline, ATP III, into the system. We will not only aim to improve its functions accordingly, but also make it cover a wider spectrum of diseases by implementing more guidelines into CPOE in the future.

There are still some spaces for further improvements for the CAGES. We will strive to build a better CAGES, which will analyze patient’s previous examining data and come out with a solution automatically. Then, combine the solution with other medical treatments that the patient is having at the moment to generate a final result for physicians as a diagnosing reference. Once it is accomplished, it would greatly reduce the time of diagnosis and errors of numerical analysis by humans.

5. Conclusion

In conclusion, the implementation of the “home growing” CAGES in a medical center is a start on improving patient safety and quality. Our experience with this process can become the model for further improvement of the CPOE. This study revealed that 65% of the patients reached the LDL-C goal in 1 year. It is better than other study with the report of 50% reached the LDL-C goal [18,25]. For those who prescribed through CAGES, 74% attained their low-density lipoprotein cholesterol goal in 1 year. For those who with CAGES exited, 57% reached the LDL-C goal. The odds ratio is 2.1 (1.2, 3.8) ($p=0.022$). The mean of days to attain the LDL-C goal level after initiation of statin therapy was 175 ± 98 days which is compatible to 189 ± 90 days in other study [18].

We conclude that a CPOE with CDSS integrated may increase the proportion of high risk hyperlipidemia patients to reach the LDL-C goal. However, data also showed the total prescribing time may increase.

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REFERENCES

- [1] L.T. Kohn, J.M. Corrigan, M.S. Donaldson, *To Err is Human: Building a Safer Health System*, Institute of Medicine, National Academy Press, Washington, DC, 2000.
- [2] S.S. Lyons, T. Tripp-Reimer, B.A. Sorofman, J.E. DeWitt, B.J. BootsMiller, T.E. Vaughn, B.N. Doebeleing, Information technology for clinical guideline implementation: perceptions of multidisciplinary stakeholders, *J. Am. Med. Inform. Assoc.* 12 (2005) 64–71.
- [3] M.J. Field, K.N. Lohr, *Guidelines for Clinical Practice: From Development to Use*, Institute of Medicine, National Academy Press, Washington, DC, 1992.
- [4] L. Olsen, D. Aisner, J.M. McGinnis, *The Learning Healthcare System: Workshop Summary (IOM Roundtable on Evidence-Based Medicine)*, Institute of Medicine, National Academy Press, Washington, DC, 2007.
- [5] E.A. McGlynn, S.M. Asch, J. Adams, J. Keesey, J. Hicks, A. DeCristofaro, E.A. Kerr, The quality of health care delivered to adults in the United States, *N. Engl. J. Med.* 348 (26) (2003) 2635–2645.
- [6] W.M. Tierney, J.M. Overhage, B.Y. Takesue, L.E. Harris, M.D. Murray, D.L. Vargo, C.J. McDonald, Computerizing guidelines to improve care and patient outcomes: the example of heart failure, *J. Am. Med. Inform. Assoc.* 2 (1995) 316–322.
- [7] P.C. Tang, C.Y. Young, Active guidelines: integrating web-based guidelines with computer-based patient records, in: *AMIA Annu. Symp. Proc.*, 2000, pp. 843–847.
- [8] M.K. Goldstein, B.B. Hoffman, R.W. Coleman, M.A. Musen, S.W. Tu, A. Advani, R. Shankar, M. O’Connor, Implementing clinical practice guidelines while taking account of changing evidence: ATHENA DSS, an easily modifiable decision-support system for managing hypertension in primary care, in: *AMIA Annu. Symp. Proc.*, 2000, pp. 300–304.

- [9] A.X. Garg, N.K. Adhikari, H. McDonald, M.P. Rosas-Arellano, P.J. Devereaux, J. Beyene, J. Sam, R.B. Haynes, Effects of computerized clinical decision support systems on practitioner performance and patient outcomes: a systematic review, *JAMA* 293 (10) (2005) 1223–1238.
- [10] Expert panel on detection, evaluation, and treatment of high blood cholesterol in adults. Executive summary of the third report of the national cholesterol education program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III), *JAMA* 285 (2001) 2486–2497.
- [11] R.S. Safeer, P.S. Ugalat, Cholesterol treatment guidelines update, *Am. Fam. Phys.* 65 (2002) 871–880.
- [12] P.E. McBride, National cholesterol education program, perspectives: the NCEP ATP III guidelines—friend or foe? *Prev. Cardiol.* 5 (2002) 152–155.
- [13] Third report of the National Cholesterol Education Program (NCEP). Expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III) final report, *Circulation* 106 (2002) 3143–3421.
- [14] K.V. Nair, J.J. Saseen, Quality assessment of dyslipidemia in managed care: current best evidence should be used to benchmark quality, *Ann. Pharmacother.* 40 (1) (2006) 124–127.
- [15] L.J. Mosca, Optimal management of cholesterol levels and the prevention of coronary heart disease in women, *Am. Fam. Physician* 65 (2002) 217–226.
- [16] S.M. Grundy, Prevention of coronary heart disease through cholesterol reduction, *Am. Fam. Physician* 55 (1997) 2250–2258.
- [17] S.M. Grundy, J.I. Cleeman, C.N. Merz, H.B. Brewer Jr., L.T. Clark, D.B. Hunnighake, R.C. Pasternak, S.C. Smith Jr., N.J. Stone, Implications of recent clinical trials for the National Cholesterol Education Program Adult Treatment Panel III guidelines, *Circulation* 110 (2) (2004) 227–239.
- [18] J.S. Schultz, J.C. O'Donnell, K.L. McDonough, R. Sasane, J. Meyer, Determinants of compliance with statin therapy and low-density lipoprotein cholesterol goal attainment in a managed care population, *Am. J. Manag. Care.* 11 (5) (2005) 306–312.
- [19] S. Eslami, A. Abu-Hanna, N.F. de Keizer, Evaluation of outpatient computerized physician medication order entry systems: a systematic review, *J. Am. Med. Inform. Assoc.* 14 (4) (2007) 400–406.
- [20] T.A. Jacobson, Reaching National Cholesterol Education Program Goals: a managed care approach to improving hyperlipidemia disease management outcomes. Introduction, *Am. J. Med.* 110 (Suppl. 6A) (2001) 1S–2S.
- [21] T.H. Lee, J.I. Cleeman, S.M. Grundy, C. Gillett, R.C. Pasternak, J. Seidman, C. Sennett, Clinical goals and performance measures for cholesterol management in secondary prevention of coronary heart disease, *JAMA* 283 (1) (2000) 94–98.
- [22] C. Carroll, P. Marsden, P. Soden, E. Naylor, J. New, T. Dornan, Involving users in the design and usability evaluation of a clinical decision support system, *Comput. Methods Prog. Biomed.* 69 (2) (2002) 123–135.
- [23] R. Goud, A. Hasman, N. Peek, Development of a guideline-based decision support system with explanation facilities for outpatient therapy, *Comput. Methods Prog. Biomed.* 91 (2) (2008) 145–153.
- [24] M. Persson, J. Bohlin, P. Eklund, Development and maintenance of guideline-based decision support for pharmacological treatment of hypertension, *Comput. Methods Prog. Biomed.* 61 (3) (2000) 209–219.
- [25] E.S. Parris, D.B. Lawrence, L.A. Mohn, L.B. Long, Adherence to statin therapy and LDL cholesterol goal attainment by patients with diabetes and dyslipidemia, *Diabetes Care* 28 (3) (2005) 595–599.